

AD-A990 393

WALTER REED ARMY INST OF RESEARCH WASHINGTON DC
RAPID TRANSMERIDIAN DEPLOYMENT: COGNITIVE PERFORMANCE AND CHRON--ETC(U)
JUN 80 R C GRAEBER, B N CUTHERBERT, H C SING

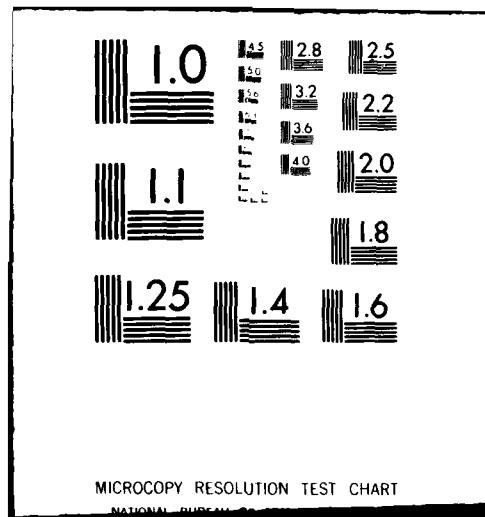
F/G 6/19

UNCLASSIFIED

NL

1 of 1
AII
AIA 2515

END
DATE FILMED
11-80
DTIC



AD A090393

GRAEBER, CUTHBERT, SING
SCHNEIDER, & SESSIONS

(11) Jun 80

(12) 15

(6) RAPID TRANSMERIDIAN DEPLOYMENT: COGNITIVE PERFORMANCE AND
CHRONOBIOLOGIC PROPHYLAXIS FOR CIRCADIAN DYSCHRONISM

(10) R. CURTIS / GRAEBER CPT, MSC
BRUCE N. / CUTHBERT CPT, MSC
HELEN C. / SING MRS.
ROBERT J. / SCHNEIDER MAJ, MSC
G. RUFUS / SESSIONS MAJ, MSC
WALTER REED ARMY INSTITUTE OF RESEARCH
WASHINGTON, D. C. 20012

JUN 1980

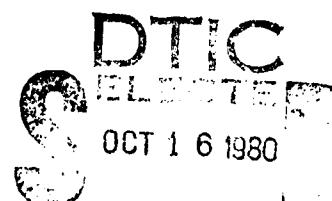
Rapid deployment of combat units to overseas locations is a primary concern of today's strategic planners. Such movements require the airlifting of units across multiple time zones. Numerous studies have documented the adverse physiological and behavioral consequences accompanying the rapid crossing of three or more time zones (1). These effects result from the requirement that the body must adjust its circadian rhythms to the new local time.

Under normal conditions, these daily cycles are synchronized by the external Zeitgebers (i.e., time-givers) of the local environment. The sudden shifting of these Zeitgebers causes the shifting at different rates of the body's physiological, biochemical, and behavioral rhythms. While some circadian rhythms adjust quite rapidly, others adjust very slowly. Consequently, the passenger's circadian system is not only out of synchrony with the environment but is also internally desynchronized. It is the latter condition, circadian dyschronism, which is particularly responsible for the fatigue and malaise typically reported as "jet lag" during the first several days following rapid transmeridian flight.

While the physiological and behavioral consequences of such flights are a common experience for airline travellers, their impact poses a potentially serious problem for troops required to display maximal combat effectiveness upon arrival at a hostile destination. The high-level cognitive performance required by the modern sophisticated battlefield may only serve to exacerbate the problem. Any

DDC FILE COPY

(101)



73

This document has been approved
for public release and sale; its
distribution is unlimited.

368450

A

80 10 16 048

GRAEBER, CUTHBERT, SING
SCHNEIDER, and SESSIONS

reduction of the adverse effects of rapid deployment would enhance combat readiness. Consequently, we designed a set of experiments to test a series of chronobiologic countermeasures (CM) which may hasten physiological and behavioral adaptation to new time zones.

Previous attempts to develop chronobiotics have not been successful. These efforts were limited to the use of a pharmacologic agent, i.e., a corticosteroid or a combined tranquilizer and central neurotransmitter depletor (2,3). In contrast, we chose to manipulate a number of different Zeitgebers simultaneously. Selection of specific CMs was based upon their suitability to the operational requirements of emergency military airlifts and their potential chronobiological effectiveness. Hence, control of the following variables was established: mealtiming, dietary constituents, caffeine and theophylline consumption, light-dark (LD) cycle, rest-activity pattern, and social-psychological time cues.

Support for the potential effectiveness of these interventions are found in the current chronobiologic literature. Ehret and his colleagues (4) have demonstrated that injections of methylated xanthines i.e., theophylline or caffeine, in rats can advance or delay the daily maximum for body temperature. If they are administered just before or during the early active phase of the circadian cycle (i.e., rising body temperature), a phase delay results, whereas if they are administered during the late active, early inactive phase (i.e., just before or after the thermal peak), a phase advance results. These investigators have also induced more rapid phase adjustment of the temperature rhythm to a shift in LD cycle by (a) fasting a rat on the day prior to the shift and (b) restoring food coincidental with the first active phase of the new LD cycle. Presumably, this chronobiotic effect is mediated by the depletion of liver glycogen during the fast followed by the reinitiation of feeding at the chronotypically appropriate time in the revised LD cycle. Others have demonstrated the importance of mealtiming as a synchronizer of circadian rhythms in humans (5).

Related work by Wurtman and Fernstrom (6,7) forms the basis of the dietary manipulations. They have shown that fasted rats exhibit a significant increase in brain tryptophan and serotonin within 1 hr. after a high carbohydrate, low protein meal. The effect is mediated by an increase in serum tryptophan elicited by insulin secretion. Fasted rats also manifest a rapid increase in brain catecholamine levels, particularly norepinephrine, following a meal rich in protein. This enhanced catecholamine synthesis can be traced directly to increases in brain tyrosine levels, the amino acid precursor of these neurotransmitters. Since a dramatic rise in brain

(102)

| | |
|--------------|--------------------|
| Printed Name | Avrilin City Sales |
| Address | Atlanta, Georgia |
| Dist | Special |
| A | |

GRAEBER, CUTHBERT, SING,
SCHNEIDER, and SESSIONS

catecholamine levels occurs at the onset of the active phase of the circadian rest-activity cycle and is associated with increased alertness (8), consuming high-protein meals in the morning and at lunchtime on the day of arrival should facilitate the rise in brain catecholamines appropriate to the active phase of the shifted circadian cycle. Conversely, a large, high-carbohydrate dinner eaten at a time in synchrony with the destination populace should facilitate the increase in brain serotonin which typically precedes sleep and therefore should hasten sleep adjustment.

Aschoff's group (1) has used an underground bunker to demonstrate the expected importance of the LD and rest-activity cycles as synchronizers of human circadian rhythms; however, their studies have also revealed the special role of social interaction in determining the speed of phase adjustment to shifted LD schedules. Similarly, post-flight participation in outdoor group activities can hasten the adaptation process following transmeridian flight (9).

In designing "jet lag" CMs for eastward deployment, we combined some of Ehret's (4) suggestions with manipulation of the factors just described. The operational requirements of a potential large-scale emergency military airlift limited the extent and duration of experimental interventions to those which could be instituted on the day of departure and carried out with minimal disruption to mission accomplishment. Likewise, in both studies described herein, operational considerations required that data collection be restricted to relatively few days before and after the flight with minimal interference in the subjects' ability to carry out their military duties. The first study evaluated the effectiveness of the CMs on troops being permanently transferred via chartered commercial airliners from Ft. Hood, TX, to W. Germany in the fall of 1978. The second study attempted to validate the CMs under more realistic combat conditions by focusing on troops from Ft. Riley, KS, being airlifted on USAF C-141 aircraft to participate in REFORGER '79 during the winter. The latter study also examined the effects of deployment on cognitive performance without the CMs.

EXPERIMENT 1

Subjects. The sample comprised 179 soldiers (18 to 44 years old) from the 2nd Armored Div. transferring as a unit from Ft. Hood, TX, to W. Germany. Eighty-four of the subjects flew on one aircraft and followed the CM procedures; the remaining 95 control subjects deployed on a second plane. Both airliners departed the U.S. midday and arrived in Germany early the next morning, a time advance of 6 hrs.

GRAEBER, CUTHBERT, SING,
SCHNEIDER and SESSIONS

Procedure. Organismic adjustment following flight can be conceptualized into three response classes: physiological activity, subjective reports of well-being, and work performance. While the latter is of paramount concern for military planning, the first two are obviously important in determining ultimate levels of efficiency. Thus, all three areas must be considered in a comprehensive evaluation of circadian dyschronism. Oral temperature was the physiological parameter assessed on all subjects, while a sub-sample of 15 soldiers in each group was studied more intensively. The latter completed self-report scales consisting of a fatigue checklist (10) and a diary of all activities. Performance tests comprised a four-choice reaction time task and an arithmetic test of summing successive pairs of single-digit numbers in a column of 50. Subjects in these "intensive" subgroups were selected from troops living in the barracks and were tested every 4 hrs. around-the-clock for 4 days two weeks prior to departure. Pre-flight temperature measurements for the remaining subjects, who lived off-post, were taken only during their normal duty hours at 0800, 1200, and 1600 CDT.

The CM procedures for the experimental group were initiated on the morning of departure. Subjects were restricted to a light, low carbohydrate breakfast with fruit juice, milk, and decaffeinated coffee; in fact, the majority ate nothing. Napping was prohibited throughout the day. Upon boarding the aircraft, they were welcomed first in German and then instructed by the Sergeant Major to set their watches ahead 6 hrs. since henceforth the unit would function on German time. A light "supper" was announced and served at 1745 CET (1145 CDT). It consisted of a ham and cheese sandwich, a small salad, cheese, and fresh fruit. No caffeinated beverages or sweetened soft drinks were allowed. Instead, milk, unsweetened fruit juices, and "Gatorade" were available. At 2200 CET the subjects were given 100 mg of dimenhydrinate to induce drowsiness. At 2300, the cabin lights were turned off, and everyone was instructed to sleep until 0405 CET when the cabin lights were turned on. Hot washcloths were distributed, and subjects were told to stretch, interact, and move about. A high-protein breakfast, including a 6 oz. steak and a two-egg cheese omelet, was served at 0430, with second helpings available. Consumption of caffeinated beverages was encouraged since the subjects were now on the downslope of their U.S. time-referenced circadian temperature cycle. The flight landed at 0630, and the remainder of the day was largely spent unpacking at the training base following a 90 min. bus ride from the airport. Napping was prohibited throughout the first day until 1800 to prevent reversion to U.S. time.

Control subjects, in contrast, followed a normal airline

**GRAEBER, CUTHBERT, SING,
SCHNEIDER and SESSIONS**

routine. They ate a hot lunch and dinner on the aircraft at the usual U.S. times, plus a breakfast snack at 0810 CET. No alcoholic beverages were permitted. Although the cabin lights were turned off from 0215 until 0550 CET, individual reading lights were available and no constraints were placed on the subjects' activities. These subjects were allowed to nap whenever duties permitted during departure preparations and following arrival at the training base.

For the next six days, all subjects were housed in barracks and tested every 4 hrs. around-the-clock. Only light duties were assigned with no physical training or heavy labor.

Results. The most readily apparent evidence for CM effectiveness was seen in the self-reports. Experimental subjects reported significantly less fatigue during the first 24 hrs. in Germany than the control subjects ($p < 0.05$, t-test), and in fact showed little change from baseline (Fig. 1). Greater fatigue for the control subjects is also indicated by the fact that they slept longer than the CM subjects for the first two days in Germany (Fig. 2). This difference was significant even when sleep before 1800 on day 1 was excluded from the analysis (4.4 vs. 8.1 hrs., $p < 0.005$, t-test) in order to remove the potential bias resulting from the CM subjects not being allowed to nap during the day. In-flight observations demonstrated that the average amount of sleep on the plane was 5.5 hrs. for each group. It was the timing of sleep that differentiated the two groups.

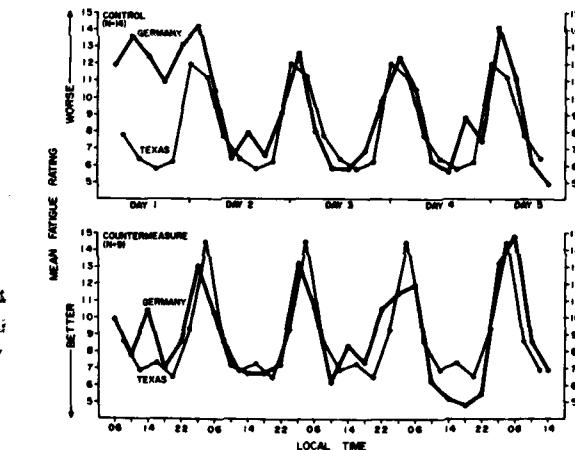


Fig. 1. Post-flight fatigue ratings compared to phase-shifted (+6 hrs.) 4-day mean ratings in Texas. Seven subjects omitted due to contradictory responses or loss of book.

GRAEBER, CUTHBERT, SING
SCHNEIDER and SESSIONS

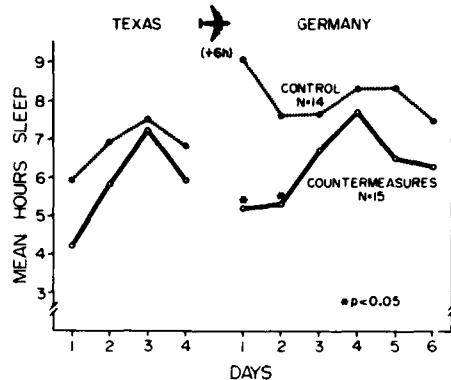


Fig. 2. Duration of daily sleep before and after deployment.

Support for the hypothesis of faster adaptation with the CMs is also provided by the oral temperature data. However, the interpretation of these results is limited by the lack of a 24-hr. baseline for the large groups and the relatively short five-day measurement period in Germany. As shown in Fig. 3, the curves of group mean temperature exhibited very rapid initial adaptation to the new time zone. Inspection of Fig. 3 suggests that, compared to the control group, the shape and amplitude of the CM function more closely approximates that of the intensive groups' baseline for the first two days in Germany. Both large groups appear rather similar thereafter. Whether there is a difference in the rate of final adaptation of the two groups can not be determined since data collection terminated after five days.

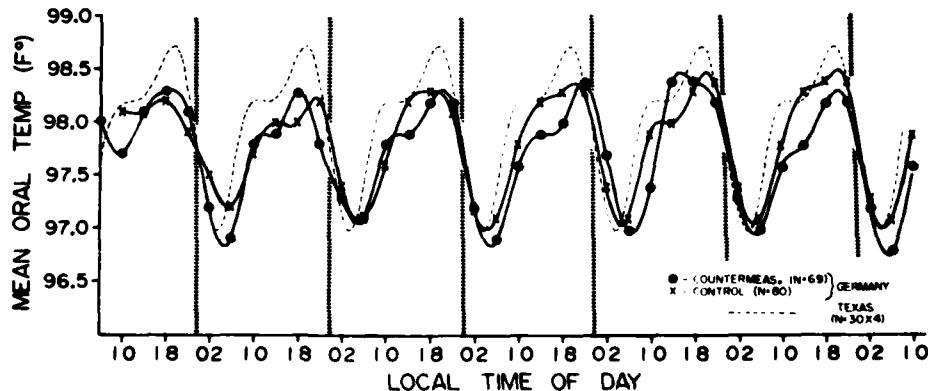


Fig. 3. Spline-fit functions of large groups' mean post-flight temperature compared to phase-shifted estimate of pre-flight rhythm based on combined small groups in Texas.

GRAEBER, CUTHBERT, SING,
SCHNEIDER and SESSIONS

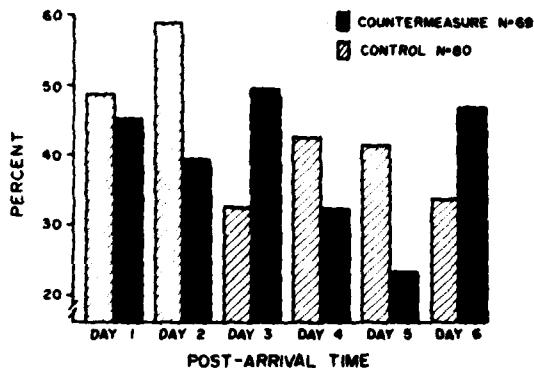


Fig. 4. Percent of subjects whose thermal acrophase indicated lack of phase adaptation (see text).

Group means tend to minimize the day-to-day variation of individuals and may obfuscate the oscillatory nature of the adjustment process by implying a smooth, gradual transition. Consequently, assessment of rhythmic structure was made by subjecting the data to a complex demodulation (CD) analysis (11) which outputs a pseudo-sinusoidal estimate of the times of the circadian maximum and minimum for each subject per day. Figure 4 shows the results of one compilation of these analyses. It depicts the daily percentage of subjects whose estimated acrophase (i.e., peak time) fell outside a one standard deviation range about the pre-flight mean acrophase (1713 ± 2.9 hrs) of the combined intensive groups. It is evident that phase adaptation proceeded irregularly and cyclically, with an approximate 3-day cycle. Unfortunately, the data terminate before any firm conclusions can be drawn regarding differential overall adaptation rates between the two large groups.

The group mean temperature curves for the intensive groups varied in a different fashion than those for the large groups, particularly during the first four days. The variability from day to day in both amplitude and phase may reflect the small number of subjects, the sleep-disrupting schedule, or chance. Adaptation of mean temperature appeared to be largely complete by day 6.

A CD analysis of each subject's temperature data provided individual estimates of the circadian and ultradian components. Due to the limitation of a 4-hr. sampling rate, the latter comprised frequencies of two and three cycles per day. Total energy may be represented by the sum of all frequencies, while shifts in energy may occur among the various components during periods of adaptation. Figure 5 indicates that the CM subjects maintained a relatively higher percen-

GRAEBER, CUTHBERT, SING,
SCHNEIDER and SESSIONS

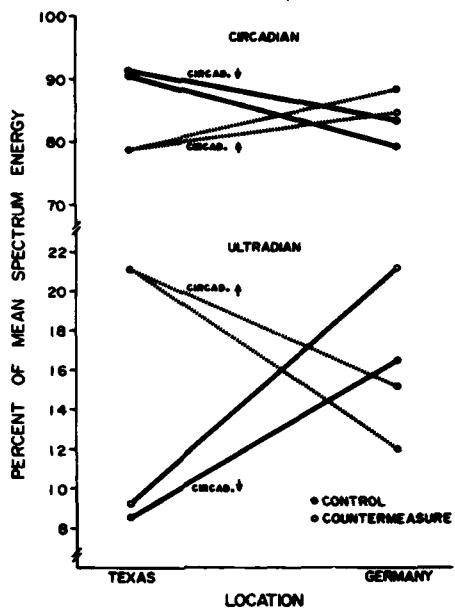


Fig. 5. Shifts in spectral energy of thermal rhythms after deployment. Subjects have been divided into those who increased (Control=7, CM=6) and those who decreased (Control=8, CM=9) circadian energy.

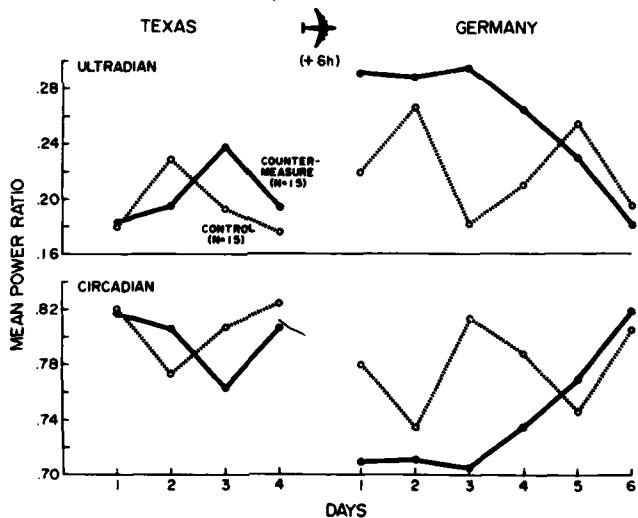


Fig. 6. Daily mean power ratios of thermal rhythms. Control group components differ from CM components on days 1, 3, and 4 in Germany and on day 3 in Texas ($p < 0.001$, t-test on arc sine transforms).

GRAEBER, CUTHBERT, SING,
SCHNEIDER and SESSIONS

tage of ultradian energy post-flight regardless of whether they increased or decreased the spectral strength of the circadian component. This effect is dissected in Fig. 6, where the mean power ratios are plotted daily for each group. Both groups exhibited moderate day-to-day variability in Texas, and deviated even more following the flight. The CM subjects, however, changed smoothly and gradually back to the baseline from initial days of relatively high ultradian energy, while the control group varied erratically.

Because older individuals adapt with greater difficulty to altered work-sleep schedules (15), two subgroups of older subjects (≥ 30 yrs.) were drawn for comparison. In Fig. 7 it is evident that the CMs were particularly efficacious in preserving the amplitude and phase of their circadian temperature rhythm. Obvious differences between the control and CM groups disappeared by day 3.

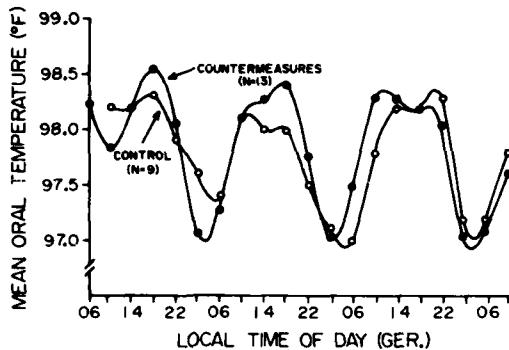


Fig. 7. Spline-fit functions of post-flight temperatures in older soldiers.

A final point concerns the mean daily temperature averaged over all times. As others have reported (13), this value was suppressed following the flight (Fig. 8). Although the group means were identical in Texas, the control group exhibited a consistently (but not significantly) greater decrease after day 1 in Germany. This finding is a further suggestion of the beneficial effects of the CMs.

Assessment of the third component of interest, test performance, was limited. The addition task exhibited the close covariation with body temperature which has been reported frequently for tasks of this type. However, no group differences were detected following the flight, performance levels in both groups remaining virtually unchanged. Data from the 4-choice reaction task, currently being transferred from tape to computer, are unavailable at this time.

GRAEBER, CUTHBERT, SING,
SCHNEIDER and SESSIONS

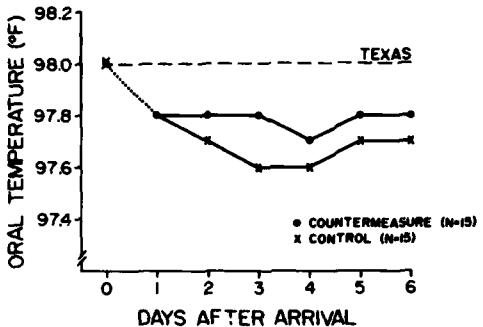


Fig. 8. Mean daily post-flight oral temperatures compared to each group's overall mean daily temperature in Texas.

EXPERIMENT 2

The second experiment was designed to confirm the initial findings under more rigorous field conditions. Secondly, recognizing the critical importance of post-deployment cognitive functioning, we collected additional data to evaluate performance changes as a function of age. The study was carried out during winter REFORGER '79, with snow and extreme cold both in the U.S. and Germany.

Subjects. The CMs were tested on 120 subjects from an artillery battalion deployed on 4 aircraft: two each for the CM and control groups. Sixty subjects were selected from a maintenance battalion for the investigation of age effects. The "young" (N=29, mean age 21.0 yrs) and the "older" (N=29, mean age 34.2 yrs.) subjects deployed on several different aircraft with no CM treatment.

Procedure. Training and baseline testing were carried out for 4 days during the week immediately before departure from Ft. Riley, with three daily test periods corresponding to breakfast (0800), lunch (1200), and dinner (1630) times. No physiologic measures were taken. Oral temperature, the only feasible choice, would have been unreliable due to the weather. The self-report fatigue scale and the diary of the first study were employed along with scales for self-rating the abilities to concentrate, make decisions, reason clearly, and process information.

Direct assessment of performance was expanded considerably, although operational requirements limited testing of the CM group to one 3-min. task. This task, the "griddle", required subjects to encode and decode simulated map coordinates using an alphanumeric con-

GRAEBER, CUTHBERT, SING,
SCHNEIDER and SESSIONS

version table. However, the test battery for the other 60 subjects included the griddle, as well as the trails test of visuospatial search, a logical reasoning task, letter cancellation, and short-term word recall. The battery was printed in a pocket-sized booklet and required about 20 min. to complete, at the end of which the subjects rated their overall performance. A technical specialist supervised the taking of the time-limited tests.

The troops deployed on USAF C-141 transports configured in four columns of webbed seats, a cramped arrangement which made sleeping difficult. The CMs mimicked the earlier procedures as much as possible, but were modified to conform to USAF schedules, standardized in-flight meals, seating, etc. All other subjects followed standard USAF cabin procedures.

Following deployment (+7hrs.), the troops were tested for 3 to 5 days in large tents which were poorly illuminated and heated. Four test sessions were held daily on the same schedule as in the U.S. except that a night test was added at 2100 hr.

Results. The self-report data provided the strongest support for CM effectiveness. Figure 9 shows that, while both groups experienced higher than normal fatigue after arrival, CM subjects were significantly lower than controls for the first two days in Germany ($p < 0.05$, t-test). Both groups failed to return to baseline levels following partial recovery on day 3. A very similar pattern of results appeared in the four self-rating scales of information processing, etc. The CM subjects exhibited significantly smaller decrements in self-rated effectiveness for the first two days, followed by a partial recovery (Fig. 10). The sleep data were essentially equivocal in Germany because the nature of the subjects' duties precluded ad libitum sleep.

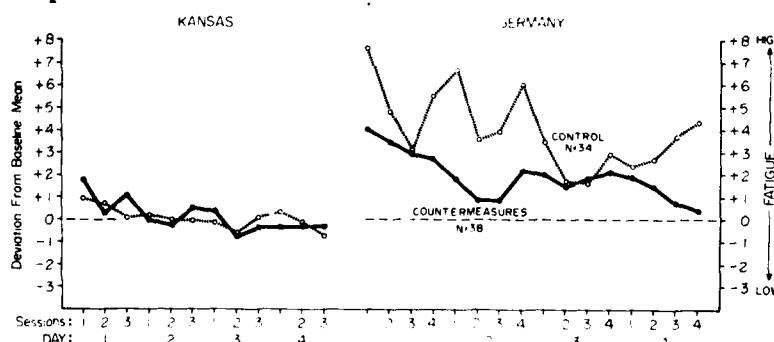


Fig. 9. Effect of CMs on self-rated fatigue in Exp. 2.

GRAEBER, CUTHBERT, SING,
SCHNEIDER and SESSIONS

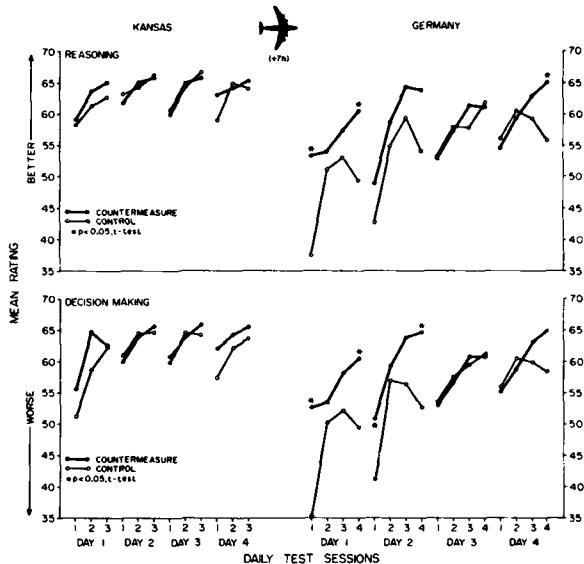


Fig. 10. Influence of CMs on self-rated cognitive abilities.

The number of items correct on the griddle test dropped 9.5% for the CM group and 12.8% for the control group on the first day following deployment, but this difference was not significant (Fig. 11). Gradual recovery occurred over the next three days. Stable accuracy levels were maintained only by the CM group.

In general, no consistent age differences were detected for self-report items or performance scores. Both old and young groups exhibited a post-flight increase in fatigue followed by partial recovery similar to the control group. Also, regardless of location, older subjects slept 20 min. less per day than younger soldiers, but the latter reported consistently lower scores on the cognitive self-rating scales throughout the entire study.

Performance on the cognitive test battery deteriorated 10 to 27% immediately after arrival, with gradual recovery over the next 1 to 4 days depending on the task. The ordering of the severity and length of task disruption corresponds to the estimated difficulty of the tests. Logical reasoning exhibited a decrease of 20% and 27% for young and old respectively, in the mean number of items correct on day 1 in Germany; baseline levels were not regained until day 4. Griddle output decreased 12% after arrival and recovered by day 3, a performance similar to the CM subjects. Accuracy during the first two days was highest in the morning and then declined. This diurnal vari-

GRAEBER, CUTHBERG, SING,
SCHNEIDER and SESSIONS

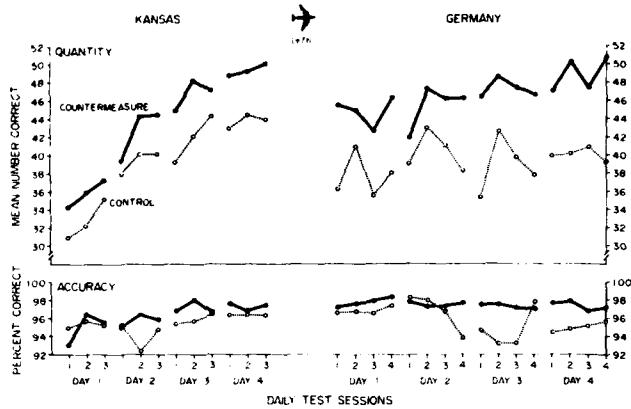


Fig. 11. Effect of CMs on encoding-decoding performance (Control N=34, CM N=38).

ability disappeared as response rate increased, so that accuracy rates displayed stable, pre-flight levels by day 4. Mean word recall dropped one word per test on day 1 and returned to baseline by day 2. No change was discerned for either group in letter cancellation speed or accuracy. The trails task, which requires the connecting of irregularly spaced targets in proper sequence, showed an unexpected post-flight improvement in performance.

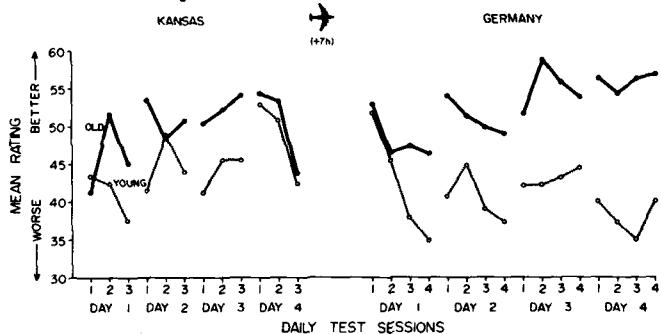


Fig. 12. Effect of age on self-rated cognitive test performance before and after deployment. Groups differ significantly ($p < 0.05$, t-test) on post-flight days (session 2) and 4 (sessions 1, 2, and 3).

Older soldiers consistently rated their overall test performance higher than younger troops (Fig. 12). This difference increased in Germany: older subjects' ratings approximately paralleled actual performance recovery, while younger soldiers persistently rated their performance lower than it was. This finding has serious morale implications for young soldiers following deployment.

GRAEBER, CUTHBERT, SING,
SCHNEIDER and SESSIONS

DISCUSSION

On the basis of self-reports the CMs reduced jet lag in both studies. Countermeasure subjects slept less on the first two nights in Germany in Experiment 1, where some degree of individual control over sleep time was possible. The sleep duration of about 5.3 hrs. for CM subjects during the first 2 nights seems unusually low, possibly because the testing procedure required awakenings at 0200 and 0600. The lower fatigue scores for these subjects make it unlikely that the sleep result was due to difficulties in falling or staying asleep.

The oral temperature evidence supports the hypothesis that CMs promote more rapid physiological adaptation. An intriguing finding is the maintenance of greater ultradian spectral energy by CM subjects during the first 3 post-flight days. The presence of significant ultradian components strongly suggests an active transitional state wherein the underlying oscillator is readjusting itself to the phase requirements of a shift in the Zeitgeber schedule.

These two studies have been less successful in demonstrating substantial CM effects with actual performance tests. The addition test used in the first study was, in retrospect, insufficiently demanding to produce substantial deficits. As seen in Experiment 2, easier tasks may show little or no impairment following time zone shifts. While accuracy in the griddle task of Experiment 2 was better maintained for CM subjects, the effect was slight, and the major dependent variable, response speed, was unaffected. Interpretation of this result is complicated by the environmental factors, which may have introduced sufficient variance to overwhelm any effect of the CMs.

Despite the limitations of the performance results, the preponderance of evidence warrants the use of the CMs in future military deployments. Although further development is needed to determine which components are particularly efficacious, the current CMs are operationally feasible and potentially valuable in maintaining combat readiness.

The expanded cognitive test battery revealed palpable deficits following the flight, but did not distinguish between older and younger subjects. Several precautions affect any conclusion that age may be irrelevant in determining the effects of rapid transmeridian deployment: (a) The age of the "older" group may have been too low to produce the difficulties typically experienced by older travelers. (b) Test difficulty was targeted toward the high-level cognitive abilities of a HQ unit. The use of troops from a maintenance battalion

GRAEBER, CUTHBERT, SING,
SCHNEIDER and SESSIONS

may have produced a "floor" effect which reduced the sensitivity of the tasks to flight-induced cognitive deficits. (c) Finally, the adverse environment may have caused excessive variance in the data and lower mean scores throughout the post-deployment observation span.

REFERENCES

1. Aschoff, J., K. Hoffman, H. Pohl, and R. Wever. 1975. Reentrainment of circadian rhythms after phase-shifts of the zeitgeber. Chronobiologia. 2:23-78.
2. Christie, G. A., and M. Moore-Robinson. 1970. Project Pegasus: some physiological effects of travel across time zones. Clin. Trials J. 7:45-55.
3. Simpson, H. M., N. Bellamy, J. Bohlen, and F. Halberg. 1973. Double blind trial of a possible chronobiotic (Quadon). Int. J. Chronobiology. 1:287-311.
4. Ehret, C. F., K. R. Groh, and J. C. Meinert. 1978. Circadian dyschronism and chronotypic ecophilia as factors in aging and longevity. Adv. Exp. Med. Biol. 108:185-213.
5. Graeber, R., R. Gatty, F. Halberg, and H. Levine. 1978. Human eating behavior: preferences, consumption patterns, and bio-rhythms. U.S. Army Natick Res. & Devel. Cmd., Tech. Rep. TR-78-022.
6. Fernstrom, J. D. 1976. The effect of nutritional factors on brain amino acid levels and monoamine synthesis. Fed. Proc. 35:1151-1156.
7. Wurtman, R. J. 1979. When -- and why -- should nutritional state control neurotransmitter synthesis? J. Neural. Transm., Suppl. 15:69-79.
8. Perlow, M. M. Ebert, E. Gordon, M. Ziegler, C. Lake, and T. Chase. 1978. The circadian variation of catecholamine metabolism in the subhuman primate. Brain Res. 139:101-113.
9. Klein, K. E., and H. M. Wegmann. 1974. The resynchronization of human circadian rhythms after transmeridian flights as a result of flight direction and mode of activity. pp. 564-570. In: L. E. Scheving, H. Halberg, and J. E. Pauly, Eds. Chronobiology. Igaku Shoin, Ltd., Tokyo.
10. Pearson, R. B., and G. E. Byars, Jr. 1956. The development and validation of a checklist for measuring subjective fatigue. School of Aviation Medicine, USAF, Randolph AFB, Texas, Report No. 56-115.
11. Walter, D. O. 1968. The method of complex demodulation. EEG Clin. Neurophysiol., Suppl. 27:53-57.

